Placental volumetry by two-dimensional sonography with a new mathematical formula: prospective study on the shell of a spherical sector model

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Abstract

We aimed to determine the utility of a new mathematical model on volumetric assessment of the placenta utilizing two-dimensional (2-D) ultrasound. Placental volumetry was performed in a prospective cross-sectional survey by virtual organ computer-aided analysis (VOCAL) with the help of a shell-off method in 346 uncomplicated pregnancies according to STROBE guidelines. Furthermore, the placental thickness, length and height were measured by 2-D technique to estimate the placental volume (EPV) based on the mathematical formula on 'the shell of the spherical sector'. Assessments of fetal size by 2-D sonography were also carried out. The data series on placental volume measured by 2-D and 3-D techniques showed a correlation of 0.86. In the first trimester, the correlation was 0.82 and the interrelation was 0.86 later during pregnancy. Placental volumetry using 'the circle shaped shell of the spherical sector' mathematical model in 2-D ultrasound technique may be introduced in everyday practice in order to screen for placenta volume deviations attributed to adverse pregnancy outcome.

Keywords: *placenta, VOCAL (virtual organ computer-aided analysis), volumetry, two-dimensional and three-dimensional ultrasound technique*

Introduction

Fetal birthweight correlates directly to placental weight at birth (Thame et al. 2001; Thame et al. 2004). A small-for-gestational-age (SGA) neonate has a placenta with reduced weight and volume compared to the appropriate-for-gestational-age (AGA) counterpart (Derwig et al. 2011; Plasencia et al. 2011) suggesting that the adequate fetal growth depends essentially on the placental expansion. Placentomegaly can be observed in case of maternal diabetes, maternal anemia, several fetal malformations (i.e. immune or non-immune hydrops foetalis) and infections (Kuhlmann and Warsof 1996; Degani 2006).

Prediction of the intrauterine growth retardation (IUGR) (Derwig et al. 2011; Thame et al 2004) as well as pregnancies with other adverse outcomes (Gassner et al. 2003; Metzenbauer et al. 2002; Odibo et al. 2011) is a major obstetrical problem (Salafia et al. 2006). Importantly, an increasing amount of evidence demonstrates that the neonatal birthweight can be predicted significantly by placental volumetry during early to mid-pregnancy (Derwig et al. 2013) using three dimensional (3-D) sonography (Collins et al. 2013; Gassner et al. 2003; Metzenbauer et al. 2002; Odibo et al. 2011; Plasencia et al. 2011; Plasencia et al. 2012; Rizzo et al. 2012). Placental volume deviation might predict chromosomal abnormalities (Gassner et al. 2003; Metzenbauer et al. 2002), growth retardation (Collins et al. 2013; Hafner et al. 1998; Hafner et al. 2006), late-onset pre-eclampsia (Hafner et al. 2006) and other complications during pregnancy (Collins et al. 2013; Hafner et al. 2006; Odibo et al. 2011; Plasencia et al. 2011, Plasencia et al. 2012; Rizzo et al. 2012; Salafia et al. 2006).

However, 3-D placental volumetry cannot be introduced in everyday practice, since it requires special skill., By contrast, 2-D technique is simpler and it is still in use to estimate placental volumetry (Azpurua et al. 2010; Costantini et al. 2012; Schwartz et al. 2010).

Despite the constant need for estimating placental volume, only one model using 3-D (Schwartz et al. 2012) has been tested so far, and solely one previous study on volumetry was dealing with 2-D technique using a mathematical model (Azpurua et al. 2010). However, placental shapes are variable (Abramowicz and Sheiner 2008), and, as a consequence, measuring the thickness or width of placenta provides contradictory results, which are non-specific (Abramowicz and Sheiner 2008; Salafia et al. 2006) and cannot predict fetal birthweight or perinatal complication satisfactorily (Costantini et al. 2012; Elchalal et al. 2000; Salafia et al. 2006).

Our aim was to determine the applicability of a newly developed mathematical formula based on modeling the placenta as 'the shell of the spherical sector' (Figure 1a-d and 2), which was created by one of the authors (Z.K.). The validation of this model was carried out via measuring maximal height, length and thickness of placental series by 2-D sonography and calculation of volumes based on this formula. Correlation analysis of the dataset of estimated placental volumes (EPV) and measured placental volumes (MPV) were conducted utilizing 3-D technique (Odibo et al. 2011; Pomorski et al. 2012; Rizzo et al. 2012) in normal pregnancies. A further aim was to compare the dependence of the placental volumes upon the gestational age.

Methods

This is a prospective observational study of a consecutive series of 346 healthy women with singleton pregnancy who underwent ultrasound examination from 9^{+0} to 28^{+2} weeks of gestation at the Department of Obstetrics and Gynecology of the University of Szeged, Hungary. At our unit, three ultrasound scans are routinely offered to all women (at 11-13 weeks of gestation for nuchal translucency screening, at 16-22 weeks of gestation to detect any fetal abnormalities and at 24-28 weeks of gestation to assess fetal growth and development). All women attending these scans were invited to participate in this research study between 1 September and 25 December, 2011. The study was approved by the Ethical Committee of the University of Szeged (protocol number: 135/2011). Informed consent was obtained from all participants. Three hundred and ninety participants were excluded due to pregnancy that resulted in delivery of SGA or large-for-gestational-age (LGA) neonate (i.e. the birth weight was below the 10th or above the 90th percentile, respectively), multiple pregnancy, fibroids, enlarged (>3mm) nuchal translucency from 11^{+0} to 13^{+6} weeks of gestation, fetal or neonatal structural/chromosomal anomalies, amniotic fluid anomalies (i.e. oligohydramnios), inadequate localization (i.e. placenta previa), posterior placenta or functional defect (i.e. placental abruption) or structural abnormality of the placenta (i.e. bilobed placenta, placenta with succenturiate lobe), vaginal bleedings, self-reported drugs, alcohol, caffeine or nicotine abuse, preterm birth, maternal complication during pregnancy such as preeclampsia or diabetes or chronic systematic illness, and not signing the consent form. A detailed follow-up was implemented after enrolment (i.e. giving birth at our unit). Inclusion criteria comprised a singleton pregnancy with the lack of uterine contractions while the ultrasound scan was set and the entire view of the placenta in one sweep (the way the placental length, height and thickness can be visualized in one field is presented in Figure 2). The quality of study was assured using a checklist adapted from STROBE (Strengthening the Reporting of Observational studies in Epidemiology).

Development of the mathematical model on spherical section

Azpurua et al. (Azpurua et al. 2010) have worked out a mathematical model on convex-concave shell formula (‘spherical cap’) for 2-D volume estimation of the placenta based on measuring of maximal linear length, height and thickness. Based on the idea of one of the authors (Z.K.), the placental volume was modeled by another mathematical formula of ‘the shell of the spherical sector’ involving the same measured placental parameters, but yielding other results than those of Azpurua et al. (Azpurua et al. 2010) The mathematical formula serves for the estimation of expected placental volume (Figure 1 a-d). A mathematician (H.P.) has provided the adaptable mathematical formula for our idea. The maximal placental thickness, height and length were acquired in an image illustrated in Figure 2, where placental thickness and height was perpendicular to the placental length.

Volume acquisition by two and three-dimensional techniques

All 3-D scans and the 2-D ultrasound measurements were performed by one specifically trained sonographer (A.S.) to eliminate inter-observer errors. For each patient, sonographic parameters for placental volumes and fetal weights were evaluated three times during a period of maternal apnoe and fetal rest. The average of three repeated measurements was used for each evaluation. Placentas were assessed by a standard 2-D ultrasound and placental dimensions were determined in order to obtain the optimal setting for measuring their maximal height and thickness at maximal length as linear measurements (Figure 2). Placental volumes were calculated (estimated placental volumes, EPVs) on the images where the maximal length was visualized on its longitudinal plane. Where the placenta had a substantial thickness at the edge, the caliper was placed midway between the chorionic and basal plates on both edges for maximal length. The maximal placental thickness maintaining close proximity to the perpendicularity to the placental surface and the line of maximal length was measured. Furthermore, the thickness was measured at the maximal length. For laterally located placentas slight lateral inclination of the transducer was positioned to obtain proper images. Fetal weight was calculated by the formula B of Hadlock (Hadlock et al. 1985) after measuring the necessary sonographic parameters (head circumference, abdominal circumference and femur length).

Images for 3-D determination of placental volume (measured placental volume: MPV) were also obtained after the 2-D scans. Voluson 730 ultrasound machines (GE Medical Systems, Kretztechnik GmbH&Co OHG, Austria) equipped with a multifrequency transabdominal convex probe (2-5 MHz) was used to acquire all images. Each sample was examined using 3-D rendering mode, in which the color and gray value information was processed and combined to present 3-D image (mode cent; smooth: 4/5; FRQ: low; quality: 16; density: 6; enhance: 16; balance: 150; filter: 2; actual power: 2 dB; pulse repetition frequency: 0.9) (Rizzo et al. 2012).

The entire view of the placenta was identified by two-dimensional ultrasound investigation, and the volume box was adjusted which contained the whole placenta. The angle of volume acquisition varied between 45º and 70º according to placental size. The volume acquisition was obtained at ‘maximum’ speed and its duration was below 10 seconds keeping the probe perpendicular to the placental plate. The 3-D static volume box was placed over the entire placenta. The sweep angle was set at maximum 70º and the 3-D volumetric data were stored on a removable hard disk. The longest view of the placenta on plane ‘A’ was chosen as reference image. The same pre-established instrument settings were used in all the cases (Obstetrician/2-3 trimester). Each image was recovered from the disk in succession for processing. The stored volumes marked by outlining the contour of the placenta repeatedly after rotating its image 6 times by 30° with manual control to exclude decidua and maternal blood vessels were analyzed using the virtual organ computer-aided analysis (VOCAL) program pertaining to the computer software 4-D VIEW (GE Medical Systems, Austria, version 10.4). After the complete rotation had been finished, the placental volume was automatically calculated by the software. Intraobserver correlation coefficient was excellent (0.97 and 0.98) regarding measuring placental parameters derived by 2-D and 3-D technique, respectively.

Intraobserver reproducibility which was calculated after three consecutive measurements of the placental parameters for 2-D volumetry as well as the placental volumes using 3-D VOCAL shell-off method by the single sonographer (A.S.) exhibited excellent intraclass-coefficients of 0.99 and 0.99 (Fleiss and Cohen 1973), respectively as far as 58 participants were concerned. Additionally, the review of the medical sonographic charts of 1,000 pregnant women revealed that 56.1% of them had a placenta partially or totally on the anterior wall of the uterus (anterior or anterior+lateral/fundal), whereas 43.9% of them had a placenta on the posterior wall, indicating that somewhat less than half of pregnancies manifest themselves in this technical problem at measurement of placental volume.

Statistical analyses

Regression curve analyses were performed with regard to both first and second trimester placental volume data by Statistical Package of Social Sciences software (version 20) in order to optimize the fitting of curves to our plot. Curve estimation models were as follows: linear, logarithmic, inverse, quadratic, power, compound, S-shaped curve, logistic, growth and exponential relations (David 2005). $P<0.05$ was considered as statistically significant. The associations between placental volume dataset measured by 2-D and 3-D technique and estimated fetal weights were determined by Pearson’s correlations. A.S. was blinded for the mathematical model and she obtained technical instructions for the sonographic measurements, but all statistical analyses were performed by Z.K.

Results

Placental volume was measured by volume analysis with shell-off method using 3-D VOCAL technique and estimated with the help of the mathematical formula measuring length, height and thickness of a total of 346 pregnancies. In addition, the fetal weight was estimated from the measurements of head circumference, abdominal circumference and femur length at the same time.

The median age of enrolled pregnant women was 32 years (range: 18-43 years) and the median of the gestational age was 19 weeks (range: 9-28,3 weeks). Dataset of the measured placental volumes (MPVs) with shell-off method using 3-D technique and estimated by the mathematical formula on 'the shell of the spherical sector' (EPVs) was plotted (Figure 3). The correlation between MPVs (mean: 158 cm^3; range:31-611 cm^3) and EPVs (mean:189 cm^3; 11-922 cm^3) was highly significant ($p<0.001$) and strong ($r=0.86$). The volumes calculated from the 'spherical cap' model provided lower, but yet high and significant correlation ($r=0.80$, $p<0.001$) (Azpurua et al. 2010).

The correlation between the MPVs and EPVs during the first trimester (between 9^{+0} and 11^{+6} weeks, 29 cases) was significant ($r=0.82$, $p<0.05$) and this association was also strong ($r=0.86$) in the subgroup with mid-pregnancy (second trimester: between 12^{+0} weeks and 28^{+2} weeks, 317 cases).

The regression curve analyses revealed that all of the curve estimation models (linear, logarithmic, inverse, quadratic, power, compound, S-shaped curve, logistic, growth, and exponential) can be significantly fitted into the plotted data, but EPVs were related most significantly to gestational age in case of S-shaped curve ($p<0.001$; $r=0.758$) when the mathematical model was applied. In addition, the exponential ($p<0.001$; $r=0.717$) regression also provided robust dependency. The linear correlation appeared to provide a less appropriate, but yet significant regression both for EPVs ($p<0.001$; $r=0.572$) and for MPVs ($p<0.001$; $r=0.493$) of pregnancy (Figures 4 and 5).

The estimated fetal weight (EFW) was significantly correlated both to MPVs ($r=0.66$, $p<0.001$) and EPVs ($r=0.72$, $p<0.001$). In our dataset, the EPVs which were calculated based on the 'spherical cap' model revealed also a significant correlation ($r=0.71$, $p<0.001$). However, a reduced, but significant correlation was found between EFW as well as placental thickness ($r=0.43$, $p<0.001$) and length ($r=0.66$, $p<0.001$).

Discussion

An increasing amount of evidence has been published on the clinical significance of the placental weight at birth and the placental weight relative to fetal birth weight that is connected with feto-maternal diseases, obstetric and neonatal outcome, perinatal morbidity/mortality, childhood growth and development (Almog et al. 2011). In addition, a disproportionally small placenta is characteristic for fetal death (Haavaldsen et al. 2013; Hasegawa et al. 2011) and growth retarded fetuses have often small placentas (Almog et al. 2011). An unfavorable placental and fetal growth *in utero* predispose to diabetes, coronary heart diseases and hypertension at subsequent ages (Barker and Thornburg 2013).

Salafia et al. (2006) suggested that large placenta relative to the fetal weight might represent placental insufficiency with reduced ability to maintain fetal growth. Thus, sonographic estimation of the placental growth in addition to the fetal growth is an important perinatal predictive indicator (Gassner et al. 2003; Hafner et al. 1998; Odibo et al. 2011; Salafia et al. 2006; Thame et al. 2001; Thame et al. 2004) and might be an adjunct modality of uteroplacental flow (Rotmensch et al. 1994). These facts underline the necessity of routine placental volumetry in everyday practice. The magnetic resonance imaging (Derwig et al. 2011) or the 3-D technique are highly precise methods (Almog et al. 2011; Collins et al. 2013; Gassner et al. 2003; Metzenbauer et al. 2002; Odibo et al. 2011; Plasencia et al. 2011; Plasencia et al. 2012; Rizzo et al. 2012; Salafia et al. 2006), but they are time and money consuming and require considerable expertise.

We render a new mathematical formula based on parameters that can easily be measured by 2-D sonographic technique and correlates highly (r=0.86) to the measured placental volumes by 3-D technique. In very special cases, where the whole placenta is not visible in one ultrasound section, however both edges, thickness and height can be visualized; the placental volume can be calculated by a 2-D technique, but cannot be measured by 3-D VOCAL technique. 'The shell of the spherical sector' represents a model of a round placenta adhering to the internal surface of a sphere-like uterus. However, placental shape varies from elliptical to other irregular forms that may lead to an under/overestimated volumetry calculation. Our new formula gives a higher correlation than another 2-D mathematical formula (r=0.80) based on 'spherical cap' reported by Azpurua et al. (Azpurua et al. 2010), which is characterized by a portion of a sphere cut off by a plane. We believe that the model we provide may be of interest in the future for diagnosing and predicting maternal/fetal complications, and the follow-up of the smaller/larger placentas up to the first half of the third trimester. However, large placentas could be checked up only until the late second trimester, since their length extends to the maximal sonographic field.

In addition, we compared the placental volumetry estimation to placental volumetric measurements, and the 'spherical cap' mathematical formula showed good correlation with the measured placental volumes and weight after delivery (r=0.80). Moreover, our method was only verified by comparing 2-D to 3-D estimated volumetry datasets. Ultrasound estimations tend to have an inaccuracy of ±10-20%.The estimated placental volumes based on our model correlated significantly to the actual estimated fetal weight which corresponds to the studies stating strong correlation between placental and fetal weight both in the first and second trimester and at the delivery as well (Thame et al. 2001; Derwig et al. 2011; Hafner et al. 1998; Almog et al. 2011).

Our results suggest that placenta grows following an S-shaped (Kozinszky and Suranyi 2012) or an exponential line during gestation between 9 and 29 weeks of gestation, which is in accordance with other literature results producing S-shaped or nearly exponential placental birthweight nomograms in the third trimester (Almog et al. 2011; Thame et al. 2001; Thame et al. 2004). The placental volume increases from a median of 22 cm^3 at about 9 weeks of gestation to 490 cm^3 at about 28 weeks of gestation, which corresponds to a previous study (Derwig et al. 2011).

One of the limitations of the method is that the sector of the ultrasound probes is 45-70º, which limits the measurable placental length and this enables studying the growth of placenta dominantly until the beginning of third trimester (Hafner et al. 1998). This is in conformity with the fact that the lateral growth of the chorionic disc is to a great extent completed by 30 to 32 weeks of gestation (Craven et al. 2000). Another limitation of the 2-D and 3-D techniques for the measurements of the placenta located on the posterior uterine wall is that the echogenic shadow of the fetus might disturb the imaging of the placenta and makes the placental volumetry impossible in an increasing proportion as gestation advances from the first to third trimester.

However, the 2-D sonographic placental volumetry might be more useful as screening tool on a daily routine in the follow-up of the rate and pattern of placental growth of growth restricted fetuses and fetuses of pregnant women with preeclampsia and diabetes, which provides additional information besides fetal biometry alone or the fetal biometry and 2-D

Doppler flowmetry in combination (Derwig et al. 2011; Odibo et al. 2011). Our study might provide evidence on the possible applicability of our mathematical model in the placental volumetry, however it should be tested in pathological pregnancies in order to introduce as a general screening test in first and second trimester.

Acknowledgement

Specially thanks to Gabor Gaspar, Ph.D. for linguistic correction of manuscript.

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Legends to the figures

Figure 1a. The section of the spherical sector

Figure 1b. The mathematical formula of the shell of the spherical sector for placenta volumetry.

Figure 1c. The spherical sector

Figure 1d. The shell of a sphere

Figure 1e. The shell of a spherical sector

Figure 2. Sonographic illustration of the parameters for placenta volumetry with 2-D technique presenting the following parameters: maximal placental length, the maximal height of placenta measured perpendicular to the length and the thickness at the same point (Figure 2a). Placental volumetry measured by using volumetric analysis with shell-off method by virtual organ computer-aided analysis (VOCAL) 3-D technique (Figure 2b).

Figure 3. Measured placental volume plotted to the estimated placental volume.

Figure 4. Estimated placental volume plotted to the gestational age. The graphs depict the linear, S-curve and exponential trendlines.

Figure 5. Measured placental volume plotted to the gestational age. The graphs depict the linear, S-curve and exponential trendlines.